

SUBSTITUTE
SEQUENCE LISTING

5 (1) GENERAL INFORMATION:

(i) APPLICANT: TOCQUE, Bruno
WASYLYK, Bohdan
DUBS-POTERSZMAN,
10 Marie-Christine

(ii) TITLE OF INVENTION: ANTAGONISTS OF THE ONCOGENIC ACTIVITY OF
THE PROTEIN MDM2, AND USE THEREOF IN THE TREATMENT OF
CANCERS

15 (iii) NUMBER OF SEQUENCES: 4

(iv) CORRESPONDENCE ADDRESS:

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25 (v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
30 (D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:
(B) FILING DATE:
35 (C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: FR 96/01340
(B) FILING DATE: 02-SEP-1996

40 (vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: WO FR95/10331
(B) FILING DATE: 04-SEP-1995

45 (viii) ATTORNEY/AGENT INFORMATION:

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(C) REFERENCE/DOCKET NUMBER: ST95050-US

50 (ix) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: (610) 454-3839
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55 (2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1476 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: other nucleic acid
 (A) DESCRIPTION: /desc = "Oligonucleotide"

10 (ix) FEATURE:

(A) NAME/KEY: CDS
 (B) LOCATION: 1..1473

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

ATG	TGC	AAT	ACC	AAC	ATG	TCT	GTA	CCT	ACT	GAT	GGT	GCT	GTA	ACC	ACC	48	
Met	Cys	Asn	Thr	Asn	Met	Ser	Val	Pro	Thr	Asp	Gly	Ala	Val	Thr	Thr		
1					5				10					15			
20	TCA	CAG	ATT	CCA	GCT	TCG	GAA	CAA	GAG	ACC	CTG	GTT	AGA	CCA	AAG	CCA	96
Ser	Gln	Ile	Pro	Ala	Ser	Glu	Gln	Glu	Thr	Leu	Val	Arg	Pro	Lys	Pro		
					20				25					30			
25	TTG	CTT	TTG	AAG	TTA	TTA	AAG	TCT	GGT	GCA	CAA	AAA	GAC	ACT	TAT	144	
Leu	Leu	Leu	Lys	Leu	Leu	Lys	Ser	Val	Gly	Ala	Gln	Lys	Asp	Thr	Tyr		
					35				40			45					
30	ACT	ATG	AAA	GAG	GTT	CTT	TTT	TAT	CTT	GGC	CAG	TAT	ATT	ATG	ACT	AAA	192
Thr	Met	Lys	Glu	Val	Leu	Phe	Tyr	Leu	Gly	Gln	Tyr	Ile	Met	Thr	Lys		
					50				55			60					
35	CGA	TTA	TAT	GAT	GAG	AAG	CAA	CAA	CAT	ATT	GTA	TAT	TGT	TCA	AAT	GAT	240
Arg	Leu	Tyr	Asp	Glu	Lys	Gln	Gln	His	Ile	Val	Tyr	Cys	Ser	Asn	Asp		
					65				70			75			80		
40	CTT	CTA	GGA	GAT	TTG	TTT	GGC	GTG	CCA	AGC	TTC	TCT	GTG	AAA	GAG	CAC	288
Leu	Leu	Gly	Asp	Leu	Phe	Gly	Val	Pro	Ser	Phe	Ser	Val	Lys	Glu	His		
					85				90			95					
45	AGG	AAA	ATA	TAT	ACC	ATG	ATC	TAC	AGG	AAC	TTG	GTA	GTA	GTC	AAT	CAG	336
Arg	Lys	Ile	Tyr	Thr	Met	Ile	Tyr	Arg	Asn	Leu	Val	Val	Val	Asn	Gln		
					100				105			110					
50	CAG	GAA	TCA	TCG	GAC	TCA	GGT	ACA	TCT	GTG	AGT	GAG	AAC	AGG	TGT	CAC	384
Gln	Glu	Ser	Ser	Asp	Ser	Gly	Thr	Ser	Val	Ser	Glu	Asn	Arg	Cys	His		
					115				120			125					
55	CTT	GAA	GGT	GGG	AGT	GAT	CAA	AAG	GAC	CTT	GTA	CAA	GAG	CTT	CAG	GAA	432
Leu	Glu	Gly	Gly	Ser	Asp	Gln	Lys	Asp	Leu	Val	Gln	Glu	Leu	Gln	Glu		
					130				135			140					
60	GAG	AAA	CCT	TCA	TCT	TCA	CAT	TTG	GTT	TCT	AGA	CCA	TCT	ACC	TCA	TCT	480
Glu	Lys	Pro	Ser	Ser	Ser	His	Leu	Val	Ser	Arg	Pro	Ser	Thr	Ser	Ser		
							145			150		155		160			
65	AGA	AGG	AGA	GCA	ATT	AGT	GAG	ACA	GAA	GAA	AAT	TCA	GAT	GAA	TTA	TCT	528
Arg	Arg	Arg	Ala	Ile	Ser	Glu	Thr	Glu	Glu	Asn	Ser	Asp	Glu	Leu	Ser		
					165				170			175					

GGT GAA CGA CAA AGA AAA CGC CAC AAA TCT GAT AGT ATT TCC CTT TCC	576
Gly Glu Arg Gln Arg Lys Arg His Lys Ser Asp Ser Ile Ser Leu Ser	
180 185 190	
5	
TTT GAT GAA AGC CTG GCT CTG TGT GTA ATA AGG GAG ATA TGT TGT GAA	624
Phe Asp Glu Ser Leu Ala Leu Cys Val Ile Arg Glu Ile Cys Cys Glu	
195 200 205	
10 AGA AGC AGT AGC AGT GAA TCT ACA GGG ACG CCA TCG AAT CCG GAT CTT	672
Arg Ser Ser Ser Ser Glu Ser Thr Gly Thr Pro Ser Asn Pro Asp Leu	
210 215 220	
15 GAT GCT GGT GTA AGT GAA CAT TCA GGT GAT TGG TTG GAT CAG GAT TCA	720
Asp Ala Gly Val Ser Glu His Ser Gly Asp Trp Leu Asp Gln Asp Ser	
225 230 235 240	
20 GTT TCA GAT CAG TTT AGT GTA GAA TTT GAA GTT GAA TCT CTC GAC TCA	768
Val Ser Asp Gln Phe Ser Val Glu Phe Glu Val Glu Ser Leu Asp Ser	
245 250 255	
25 GAA GAT TAT AGC CTT AGT GAA GAA GGA CAA GAA CTC TCA GAT GAA GAT	816
Glu Asp Tyr Ser Leu Ser Glu Glu Gly Gln Glu Leu Ser Asp Glu Asp	
260 265 270	
30 GAT GAG GTA TAT CAA GTT ACT GTG TAT CAG GCA GGG GAG AGT GAT ACA	864
Asp Glu Val Tyr Gln Val Thr Val Tyr Gln Ala Gly Glu Ser Asp Thr	
275 280 285	
35 TGC ACT TCA TGC AAT GAA ATG AAT CCC CCC CTT CCA TCA CAT TGC AAC	960
Cys Thr Ser Cys Asn Glu Met Asn Pro Pro Leu Pro Ser His Cys Asn	
305 310 315 320	
40 AGA TGT TGG GCC CTT CGT GAG AAT TGG CTT CCT GAA GAT AAA GGG AAA	1008
Arg Cys Trp Ala Leu Arg Glu Asn Trp Leu Pro Glu Asp Lys Gly Lys	
325 330 335	
45 GAT AAA GGG GAA ATC TCT GAG AAA GCC AAA CTG GAA AAC TCA ACA CAA	1056
Asp Lys Gly Glu Ile Ser Glu Lys Ala Lys Leu Glu Asn Ser Thr Gln	
340 345 350	
50 GCT GAA GAG GGC TTT GAT GTT CCT GAT TGT AAA AAA ACT ATA GTG AAT	1104
Ala Glu Glu Gly Phe Asp Val Pro Asp Cys Lys Lys Thr Ile Val Asn	
355 360 365	
55 GAT TCC AGA GAG TCA TGT GTT GAG GAA AAT GAT GAT AAA ATT ACA CAA	1152
Asp Ser Arg Glu Ser Cys Val Glu Glu Asn Asp Asp Lys Ile Thr Gln	
370 375 380	
GCT TCA CAA TCA CAA GAA AGT GAA GAC TAT TCT CAG CCA TCA ACT TCT	1200
Ala Ser Gln Ser Gln Glu Ser Glu Asp Tyr Ser Gln Pro Ser Thr Ser	
385 390 395 400	
AGT AGC ATT ATT TAT AGC AGC CAA GAA GAT GTG AAA GAG TTT GAA AGG	1248

Ser Ser Ile Ile Tyr Ser Ser Gln Glu Asp Val Lys Glu Phe Glu Arg			
405	410	415	
GAA GAA ACC CAA GAC AAA GAA GAG AGT GTG GAA TCT AGT TTG CCC CTT			1296
5 Glu Glu Thr Gln Asp Lys Glu Glu Ser Val Glu Ser Ser Leu Pro Leu	420	425	430
AAT GCC ATT GAA CCT TGT GTG ATT TGT CAA GGT CGA CCT AAA AAT GGT			1344
Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly	435	440	445
10 TGC ATT GTC CAT GGC AAA ACA GGA CAT CTT ATG GCC TGC TTT ACA TGT			1392
Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys	450	455	460
15 GCA AAG AAG CTA AAG AAA AGG AAT AAG CCC TGC CCA GTA TGT AGA CAA			1440
Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln	465	470	475
480			
20 CCA ATT CAA ATG ATT GTG CTA ACT TAT TTC CCC TAG			1476
Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro	485	490	

25 (2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 491 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

35 Met Cys Asn Thr Asn Met Ser Val Pro Thr Asp Gly Ala Val Thr Thr	1	5	10	15
30 Ser Gln Ile Pro Ala Ser Glu Gln Glu Thr Leu Val Arg Pro Lys Pro	20	25	30	
40 Leu Leu Leu Lys Leu Leu Lys Ser Val Gly Ala Gln Lys Asp Thr Tyr	35	40	45	
45 Thr Met Lys Glu Val Leu Phe Tyr Leu Gly Gln Tyr Ile Met Thr Lys	50	55	60	
50 Arg Leu Tyr Asp Glu Lys Gln Gln His Ile Val Tyr Cys Ser Asn Asp	65	70	75	80
55 Leu Leu Gly Asp Leu Phe Gly Val Pro Ser Phe Ser Val Lys Glu His	85	90	95	
60 Arg Lys Ile Tyr Thr Met Ile Tyr Arg Asn Leu Val Val Asn Gln	100	105	110	
65 Gln Glu Ser Ser Asp Ser Gly Thr Ser Val Ser Glu Asn Arg Cys His	115	120	125	

Leu Glu Gly Gly Ser Asp Gln Lys Asp Leu Val Gln Glu Leu Gln Glu
 130 135 140

5 Glu Lys Pro Ser Ser Ser His Leu Val Ser Arg Pro Ser Thr Ser Ser
 145 150 155 160

Arg Arg Arg Ala Ile Ser Glu Thr Glu Glu Asn Ser Asp Glu Leu Ser
 165 170 175

10 Gly Glu Arg Gln Arg Lys Arg His Lys Ser Asp Ser Ile Ser Leu Ser
 180 185 190

Phe Asp Glu Ser Leu Ala Leu Cys Val Ile Arg Glu Ile Cys Cys Glu
 15 195 200 205

Arg Ser Ser Ser Ser Glu Ser Thr Gly Thr Pro Ser Asn Pro Asp Leu
 210 215 220

20 Asp Ala Gly Val Ser Glu His Ser Gly Asp Trp Leu Asp Gln Asp Ser
 225 230 235 240

Val Ser Asp Gln Phe Ser Val Glu Phe Val Glu Ser Leu Asp Ser
 245 250 255

25 Glu Asp Tyr Ser Leu Ser Glu Glu Gly Gln Glu Leu Ser Asp Glu Asp
 260 265 270

Asp Glu Val Tyr Gln Val Thr Val Tyr Gln Ala Gly Glu Ser Asp Thr
 30 275 280 285

Asp Ser Phe Glu Glu Asp Pro Glu Ile Ser Leu Ala Asp Tyr Trp Lys
 290 295 300

35 Cys Thr Ser Cys Asn Glu Met Asn Pro Pro Leu Pro Ser His Cys Asn
 305 310 315 320

Arg Cys Trp Ala Leu Arg Glu Asn Trp Leu Pro Glu Asp Lys Gly Lys
 325 330 335

40 Asp Lys Gly Glu Ile Ser Glu Lys Ala Lys Leu Glu Asn Ser Thr Gln
 340 345 350

Ala Glu Glu Gly Phe Asp Val Pro Asp Cys Lys Lys Thr Ile Val Asn
 45 355 360 365

Asp Ser Arg Glu Ser Cys Val Glu Glu Asn Asp Asp Lys Ile Thr Gln
 370 375 380

50 Ala Ser Gln Ser Gln Glu Ser Glu Asp Tyr Ser Gln Pro Ser Thr Ser
 385 390 395 400

Ser Ser Ile Ile Tyr Ser Ser Gln Glu Asp Val Lys Glu Phe Glu Arg
 405 410 415

55 Glu Glu Thr Gln Asp Lys Glu Glu Ser Val Glu Ser Ser Leu Pro Leu
 420 425 430

Asn Ala Ile Glu Pro Cys Val Ile Cys Gln Gly Arg Pro Lys Asn Gly
 435 440 445

5 Cys Ile Val His Gly Lys Thr Gly His Leu Met Ala Cys Phe Thr Cys
 450 455 460

Ala Lys Lys Leu Lys Lys Arg Asn Lys Pro Cys Pro Val Cys Arg Gln
 465 470 475 480

10 Pro Ile Gln Met Ile Val Leu Thr Tyr Phe Pro
 485 490

(2) INFORMATION FOR SEQ ID NO:3:

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1182 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: other nucleic acid
 (A) DESCRIPTION: /desc = "Oligonucleotide"

25 (ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 1..1179

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

ATG GAG GAG CCG CAG TCA GAT CCT AGC GTC GAG CCC CCT CTG AGT CAG 48
 Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln
 495 500 505

35 GAA ACA TTT TCA GAC CTA TGG AAA CTA CTT CCT GAA AAC AAC GTT CTG 96
 Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu
 510 515 520

40 TCC CCC TTG CCG TCC CAA GCA ATG GAT GAT TTG ATG CTG TCC CCG GAC 144
 Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp
 525 530 535

45 GAT ATT GAA CAA TGG TTC ACT GAA GAC CCA GGT CCA GAT GAA GCT CCC 192
 Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro
 540 545 550 555

50 AGA ATG CCA GAG GCT GCT CCC CCC GTG GCC CCT GCA CCA GCA GCT CCT 240
 Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Ala Pro
 560 565 570

55 ACA CCG GCG GCC CCT GCA CCA GCC CCC TCC TGG CCC CTG TCA TCT TCT 288
 Thr Pro Ala Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser
 575 580 585

GTC CCT TCC CAG AAA ACC TAC CAG GGC AGC TAC GGT TTC CGT CTG GGC 336
 Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly
 590 595 600

	TTC TTG CAT TCT GGG ACA GCC AAG TCT GTG ACT TGC ACG TAC TCC CCT		384
	Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro		
	605 610 615		
5	GCC CTC AAC AAG ATG TTT TGC CAA CTG GCC AAG ACC TGC CCT GTG CAG		432
	Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln		
	620 625 630 635		
10	CTG TGG GTT GAT TCC ACA CCC CCG CCC GGC ACC CGC GTC CGC GCC ATG		480
	Leu Trp Val Asp Ser Thr Pro Pro Gly Thr Arg Val Arg Ala Met		
	640 645 650		
15	GCC ATC TAC AAG CAG TCA CAG CAC ATG ACG GAG GTT GTG AGG CGC TGC		528
	Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys		
	655 660 665		
20	CCC CAC CAT GAG CGC TGC TCA GAT AGC GAT GGT CTG GCC CCT CCT CAG		576
	Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln		
	670 675 680		
	CAT CTT ATC CGA GTG GAA GGA AAT TTG CGT GTG GAG TAT TTG GAT GAC		624
	His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp		
	685 690 695		
25	AGA AAC ACT TTT CGA CAT AGT GTG GTG GTG CCC TAT GAG CCG CCT GAG		672
	Arg Asn Thr Phe Arg His Ser Val Val Pro Tyr Glu Pro Pro Glu		
	700 705 710 715		
30	GTT GGC TCT GAC TGT ACC ACC ATC CAC TAC AAC TAC ATG TGT AAC AGT		720
	Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser		
	720 725 730		
35	TCC TGC ATG GGC GGC ATG AAC CGG AGG CCC ATC CTC ACC ATC ATC ACA		768
	Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr		
	735 740 745		
	CTG GAA GAC TCC AGT GGT AAT CTA CTG GGA CGG AAC AGC TTT GAG GTG		816
	Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val		
40	750 755 760		
	CGT GTT TGT GCC TGT CCT GGG AGA GAC CGG CGC ACA GAG GAA GAG AAT		864
	Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn		
	765 770 775		
45	CTC CGC AAG AAA GGG GAG CCT CAC CAC GAG CTG CCC CCA GGG AGC ACT		912
	Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr		
	780 785 790 795		
50	AAG CGA GCA CTG CCC AAC AAC ACC AGC TCC TCT CCC CAG CCA AAG AAG		960
	Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys		
	800 805 810		
55	AAA CCA CTG GAT GGA GAA TAT TTC ACC CTT CAG ATC CGT GGG CGT GAG		1008
	Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu		
	815 820 825		
	CGC TTC GAG ATG TTC CGA GAG CTG AAT GAG GCC TTG GAA CTC AAG GAT		1056

Arg	Phe	Glu	Met	Phe	Arg	Glu	Leu	Asn	Glu	Ala	Leu	Glu	Leu	Lys	Asp		
830																	
																840	
GCC CAG GCT GGG AAG GAG CCA GGG GGG AGC AGG GCT CAC TCC AGC CAC															1104		
5	Ala	Gln	Ala	Gly	Lys	Glu	Pro	Gly	Gly	Ser	Arg	Ala	His	Ser	Ser	His	
	845															855	
CTG AAG TCC AAA AAG GGT CAG TCT ACC TCC CGC CAT AAA AAA CTC ATG															1152		
10	Leu	Lys	Ser	Lys	Lys	Gly	Gln	Ser	Thr	Ser	Arg	His	Lys	Lys	Leu	Met	
	860															875	
TTC AAG ACA GAA GGG CCT GAC TCA GAC TGA															1182		
	Phe	Lys	Thr	Glu	Gly	Pro	Asp	Ser	Asp								
																880	
15																	
(2) INFORMATION FOR SEQ ID NO:4:																	
	(i) SEQUENCE CHARACTERISTICS:																
20	(A) LENGTH: 393 amino acids																
	(B) TYPE: amino acid																
	(D) TOPOLOGY: linear																
25	(ii) MOLECULE TYPE: protein																
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:																
Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln																	
	1	5	10	15													
30	Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu																
	20	25	30														
35	Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp																
	35	40	45														
	Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro																
	50	55	60														
40	Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Pro																
	65	70	75	80													
45	Thr Pro Ala Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser																
	85	90	95														
	Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly																
	100	105	110														
50	Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro																
	115	120	125														
	Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln																
	130	135	140														
55	Leu Trp Val Asp Ser Thr Pro Pro Gly Thr Arg Val Arg Ala Met																
	145	150	155	160													
	Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys																

165

170

175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln
 180 185 190

5 His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp
 195 200 205

10 Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu
 210 215 220

Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser
 225 230 235 240

15 Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr
 245 250 255

Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val
 260 265 270

20 Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn
 275 280 285

Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr
 290 295 300

Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys
 305 310 315 320

30 Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu
 325 330 335

Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp
 340 345 350

35 Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His
 355 360 365

Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
 370 375 380

Phe Lys Thr Glu Gly Pro Asp Ser Asp
 385 390